

## REMARKS

### I. Status of the Application

Claims 56, 60-62, 64 and 65 are currently pending. Claims 61 and 62 remain withdrawn from consideration by the Examiner under 37 CFR 1.142(b) as being drawn to a non-elected species, there currently being allowable no generic claim. Thus, claims 56, 60, 64 and 65 remain under examination in the application.

### II. Priority/Related Applications

The Examiner has maintained objection to the applicants' priority claim, pointing out that applications 60/030,826, 09/578,282, and 08/969,227 fail to provide adequate support under 35 U.S.C. §112 for the instantly claimed application. While applicants maintain that the priority claim was entirely appropriate for the application as filed, applicants have amended the specification and deleted the priority claim in view of the instantly pending claims, obviating the Examiner's objection in this regard. Applicants thank the Examiner for pointing out the mistaken priority claim in regards to the instant claims.

### III. The Claims Are Allowable under Section 112, 1<sup>st</sup> Paragraph

The Examiner has rejected claims 56, 60, 64 and 65 under 35 U.S.C. § 112, first paragraph. In particular, the Examiner expresses concern with the breadth of the claims, from the Examiner's perspective reading on any polymer array and some undefined photobleachable compound, in view of what the Examiner characterizes as a relatively limited disclosure in the specification. While applicants respectfully disagree with any notion that the specification is unduly limited or narrow, to simply expedite prosecution of this application, applicants have amended the claims to explicitly address the Examiner's concerns in terms of the Examiner's

rejections under the 1<sup>st</sup> paragraph of section 112. In view of the amendments and arguments set forth below, applicants respectfully request that the obviousness rejection be withdrawn.

First, to address the Examiner's concern about the claims reading on any polymer array, which according to the Examiner the specification applicants have specifically narrowed the claims by way of a Markush expression such that the array of polymers is explicitly limited to a polymer array "selected from the group consisting of an oligonucleotide array and a peptide array." Claim 56 (emphasis added). As the Examiner is aware, the fabrication of oligonucleotide arrays and peptide arrays is discussed at length in the application (see description of oligonucleotide array fabrication using photolithography in application at pp. 16-18) and in the references incorporated by reference in the specification (see description of photolithographic peptide arrays in U.S. Patent No. 5,143,854, incorporated by reference at p. 16 of application.) Indeed, the Examiner has specifically indicated that the application is enabling with respect to nucleotide and peptide arrays. See Office Action of April 3, 2003 at p. 5.

Second, the Examiner has expressed concern over the term "a photobleachable compound." In particular, the Examiner objects that applicants provide inadequate guidance to one of skill in the art as to how to select such a compound, particularly in view of the scope of the previous claim, covering a method for synthesizing any polymer. Applicants have addressed this concern in two ways, again to expedite prosecution of this application. First, applicants have amended the claims to specifically require that the photobleachable compound absorb the same wavelength of light that is used to remove the photosensitive protective group, protecting the reactive group. In this regard, the claims have also been amended to specify that the photosensitive protective group has a certain wavelength of light for deprotection. This amendment specifically limits the photobleachable compound and provides exact guidance to those of skill in the art as to how to choose a photobleachable compound.

Second, as noted above, the claimed arrays no longer read on the synthesis of any array; rather the claims have been limited to oligonucleotide and peptide arrays for which specific guidance as to photosensitive protective groups and appropriate wavelengths of light for deprotection is known. (See specification and references cited therein). Moreover, the specification provides specific examples of using a photobleachable compound in the context of a protective group which is commonly used in photolithographic synthesis of oligonucleotides

and can be used in the photolithographic synthesis of peptide arrays. (See Example II, p. 31, using a CEM layer comprising a diazonium dye spun coat on to solid support bearing the photoprotective group MeNPOC.

Finally, applicants have added language to the base claim, specifying that the claimed method is directed to introducing latency into the method of synthesizing an array of polymers. In this regard, the amended claim recites "[a] method for introducing latency into the synthesis of a polymer array. . . ." This added phrase serves to further define the claim and the role of the photobleachable compound therein. As explained in the specification:

Photobleachable compounds can also be used to introduce latency. For example, when a . . . photobleachable material is used in combination with a compound such as MeNPOC photodeprotection can be slowed. In the absence of such a compound, direct photolysis of photolabile compounds such as MeNPOC exhibits linear responses to light such that deprotection rates are proportional to the amount of light absorbed. In the presence of a CEM compound comprised of a photobleachable compound, the CEM competes with the MeNPOC for the absorbancy of light. It is only after the opaque CEM has absorbed light and converted to a transparent film that the MeNPOC can then react. MeNPOC therefore lies dormant until all the CEM is bleached."

Specification at p. 13, lns. 14-24. As further explained, photobleachable compounds have been observed to "absorb stray light in the unexposed areas, thus allowing for more specific definition between exposed and unexposed regions" (p. 19, lns. 21-23) and "improve topographical sharpness." (Id., lns. 17-18).

In view of the above amendments and arguments, applicants respectfully assert that the Examiner's grounds of rejections under 35 U.S.C. § 112 have been overcome or obviated.

#### **IV. The Claims Are Non-Obvious**

The Examiner rejected claims 56, 60, 64 and 65 under 35 U.S.C. § 103(a) as being unpatentable over Pirrung et al. (US 5,143,854) in view of Zebala (US 6,159,681). Applicants respectfully traverse.

USSN 09/922,426  
Amendment in Response to Office Action dated 10/21/03

Page 7

Neither reference, whether considered alone or together, teach or disclose each and every element of the claimed invention, thus, failing the most basic tenant of obviousness. For ease of reference, applicants paraphrase the elements of Claim 56 below. Claim 56, the base claim, as presently amended, is directed to a method for introducing latency into the synthesis of a polymer array, the polymer array selected from the group consisting of an oligonucleotide array and a peptide array, on a substrate, the method having the steps of:

- a) providing a surface having one or more synthesis intermediates, the synthesis intermediates selected from the group consisting of a linker, a nucleotide, an amino acid, a peptide and an oligonucleotide, bound thereon, the synthesis intermediates having a reactive group protected from reaction by a photosensitive protecting group, the protecting group having a first wavelength of light which removes the protecting group from the reactive group;
- b) coating said surface with a substance comprising a photobleachable compound, wherein the photobleachable compound absorbs light having the first wavelength as that for deprotecting the photosensitive protecting group;
- c) irradiating at least a part of said surface with light having the first wavelength to:
  - i) bleach said photobleachable compound; and
  - ii) remove said protective group;
- d) removing said substance from said surface;
- e) reacting a subsequently added synthesis intermediate, the subsequently added synthesis intermediate selected from the group consisting of a linker, a nucleotide an amino acid, a peptide and an oligonucleotide, with the unprotected reactive group, the subsequently added synthesis intermediate having a reactive group protected from reaction by a photosensitive protecting group, the protecting group having a second wavelength of light which removes said protecting group from said reactive group, wherein said first and said second wavelengths are the same or different;
- f) recoating said surface with a substance comprising a photobleachable compound, wherein said photobleachable compound absorbs light having the second wavelength; if another synthesis intermediate is to be added; and
- g) repeating steps b) through f) or not, until the desired polymer array is obtained.

In considering obviousness under section 103, it is black letter patent law that the

combined references must disclose or render obvious each and every element of the claimed invention. Here this most basic requirement is not satisfied with respect to the claims as presently amended. In short, the obviousness rejection is based on an entirely erroneous reading of the references. Applicants respectfully request that the obviousness rejection be withdrawn.

The Examiner admits that the primary reference, Pirrung, does not disclose the claimed step of coating the array surface with a substance containing a photobleachable compound. Applicants agree. But importantly that is not the sole deficiency of Pirrung, when it is considered in view of the instantly claimed invention. There is also no teaching or disclosure in Pirrung that the photobleachable compound must absorb light of the same wavelength as that used to remove the photosensitive protecting group. Pirrung's only statement in this regard is that "[t]his contrast enhancement layer may comprise a molecule which is decomposed by light such as a quinine diazid or a material which is transiently bleached at the wavelength of interest." Pirrung at col. 14, lns. 8-11. There is no teaching or suggestion in Pirrung, including in the section quoted above, of matching the photobleachable compound by the wavelength of light it absorbs to that of the photosensitive protecting group. Thus, Pirrung is missing a second element of the claimed invention.

The instantly claimed invention also requires a step of irradiation of the surface of the array with the wavelength of light to both bleach the photobleachable compound and remove the photosensitive protective group. There is simply no teaching or suggestion in Pirrung of this element. This is a third missing element from Pirrung. Finally, there is no teaching or suggestion in Pirrung of introducing latency as required by the claims as amended.

In summary, Pirrung is absent at least four disclosures required to render the claims of the instantly claimed invention unpatentable, not just one as asserted by the Examiner. Importantly,

USSN 09/922,426

Page 9

Amendment in Response to Office Action dated 10/21/03

none of the missing disclosures of Pirrung, even is remedied by the Zebala reference.

There is no teaching or suggestion in Zabala of even the element the Examiner points out is missing from Pirrung: a step of coating the surface of an array with a compound containing a photobleachable compound. Zabala teaches applying layers of photoresists. But nowhere does Zabala teach or suggest a step of applying a coating of a photobleachable compound to an array. The Examiner refers to col. 31, lns. 23-35. However, this section makes only a vague reference to using some type of contrast enhancement layer and makes no reference to a step of coating to the surface of an array as required by the claims of the instantly claimed invention. In addition, there is no teaching or suggestion that the "contrast enhancement layer" must absorb light of the same wavelength as that used to remove the photosensitive protecting group. Nor is there any teaching or suggestion of a step of irradiation with the specified wavelength to bleach both the photobleachable compound and the photosensitive protecting group. Finally, Zabala does not teach or suggest introducing latency. Thus, Zabala does not supply any of the missing elements of Pirrung.

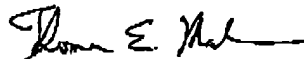
In view of the foregoing, applicants respectfully request that the Examiner's rejection of the claims at issue over 35 U.S.C. § 103(a) be withdrawn.

#### IV. Conclusion

Reconsideration and allowance of all pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (408) 731-5875.

Further, applicants respectfully request that this paper be treated as an appropriate petition for a two month extension of time. The Examiner is hereby authorized to deduct any necessary fees in this regard from applicants' deposit account no. 01-0431.

Respectfully submitted,



Thomas E. Malone

Reg. No.: 40,078

Dated: March 12, 2004

Customer No.: 22886

Affymetrix, Inc., Tel: 408/731-5000

Fax: 408/731-5392

3380 Central Expressway, Santa Clara, CA 95051